# Stroke Assessment EM Perspective

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- No financial disclosures
- No off label discussions











### Is Stroke on the Differential???

- Weakness
- Dizziness
- Numbness
- Confusion
- Sleepy
- Just Not Right
- Facial droop
- Difficulty speaking

# How high is Stroke on the differential???

- Stroke
- Sepsis
- Hypoglycemia
- Urinary Tract Infection
- Pneumonia
- MI
- CHF

S S M E N T	☐ Continuous Cardiac Monitoring ☐ Weight kg ☐ NIHSS on arrival (If Performed) ☐ Keep NPO (including meds)	Pt with signs / symptoms of stroke and symptom onset <		
T I M E	Date: :  ED TRIAGE TIME  Date: :  TIME LAST SEEN WELL	Is facility able to give tPA?  No  transfer One-call numbers on cover of packet		
D-AGNOSH-CS	CT Head w/o contrast CT Results:  No acute findings Hemorrhage New Ischemic Stroke	Yes  O – 10 min Complete Assessment and Time Sections  10 – 25 min Complete diagnostic Section 45 min Interpretation of CT		
	☐ Other: ☐ Stroke Panel - CBC, Platelets, PT-INR / PTT, Chem 8 / BMP, cardiac enzymes, glucose (bedside an option), Creat, Preg test (optional)	60 min If tPA ordered, refer to tPA Administration Order set and Treatment Section. Transfer to Tertiary Care Center  If no exclusions, consider IV tPA. May consult with neurologist on call (numbers front page)  If CT negative for hemorrhage, refer to Inclusion / Exclusion Criteria If CT positive for hemorrhage, transfer		
	☐ 12-Lead EKG	3.0 to 4.5 hr For select patients (see Complete Disposition Pre with ischemic		

# Key to making this work

- High Suspicion
- Good Process (that can be started by any team member)

# Patients Arrive by one of two mechanisms

- By Ambulance
- By Private Vehicle

### Important Information from the Ambulance

- EMS providers suspicion of Stroke
- Onset of Symptoms
- Cincinnati Stroke Scale (FAST)
- Current Medications (especially anticoagulants)

# The proof is in the Process

- Parallel processing not Serial Processing
- Process centered around must have information
- Variable outcome (ie times) indicates inconsistent Process
- Mixed messages
- Educate understanding

### Refining the Process

- Activate Stroke Code based on EMS information
- Do not off load the Patient in the ED (unless hemodynamic or respiratory instability)



- Maybe draw blood or get vitals or Do that in CT
- Off load from the ambulance cart to CT table

### Fibrinolytic Therapy for STEMI

Contraindications for fibrinolytic use in STEMI consistent with ACC/AHA 2007 Focused Updates\*

### **Absolute Contraindications**

- Any prior intracranial hemorrhage
- Known structural cerebral vascular lesion (eg. arteriovenous malformation)
- Known malignant intracranial neoplasm (primary or metastatic)
- Ischemic stroke within 3 months EXCEPT acute ischemic stroke within 3 hours
- Suspected aortic dissection
- · Active bleeding or bleeding diathesis (excluding menses)
- . Significant closed head trauma or facial trauma within 3 months

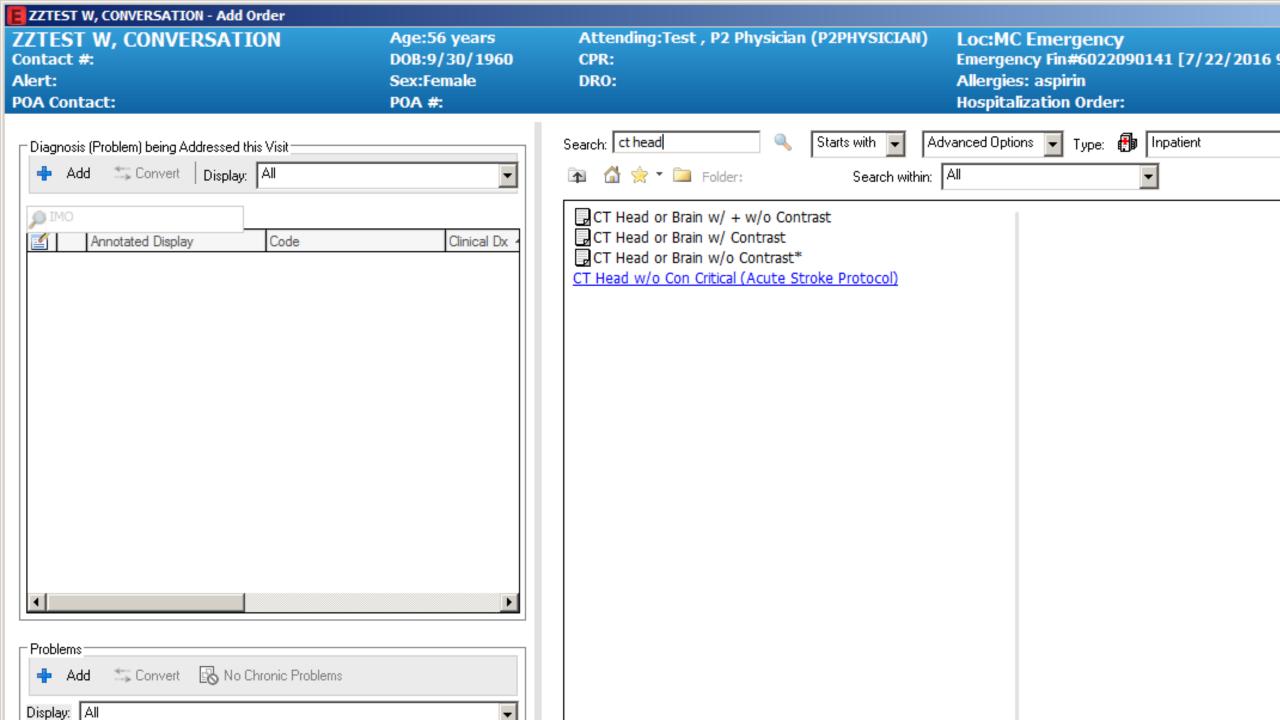
### Relative Contraindications

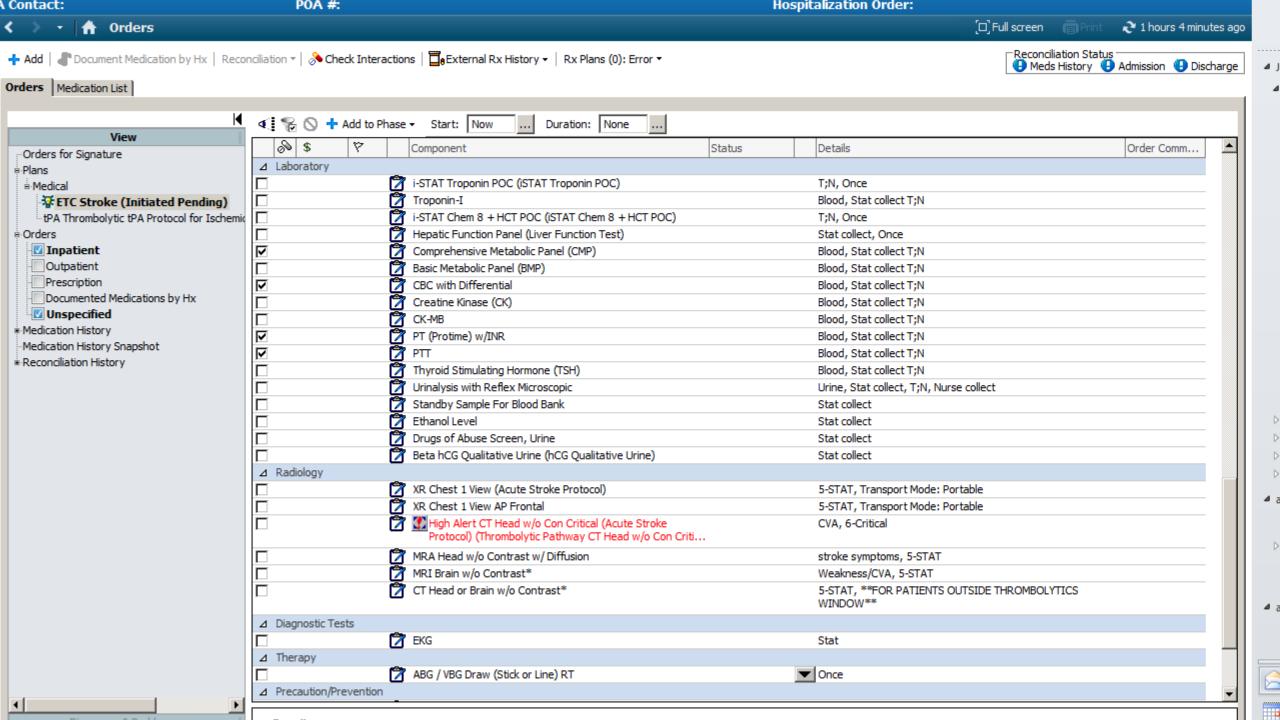
- History of chronic, severe, poorly controlled hypertension
- Severe uncontrolled hypertension on presentation (SBP >180 mm Hg or DBP >110 mm Hg)<sup>1</sup>
- History of prior ischemic stroke >3 months, dementia, or known intracranial pathology not covered in contraindications
- Traumatic or prolonged (>10 minutes) CPR or major surgery (<3 weeks)</li>
- . Recent (within 2 to 4 weeks) internal bleeding
- Noncompressible vascular punctures
- For streptokinase/anistreplase: prior exposure (>5 days ago) or prior allergic reaction to these agents
- Pregnancy
- · Active peptic ulcer
- Current use of anticoagulants: the higher the INR, the higher the risk of bleeding

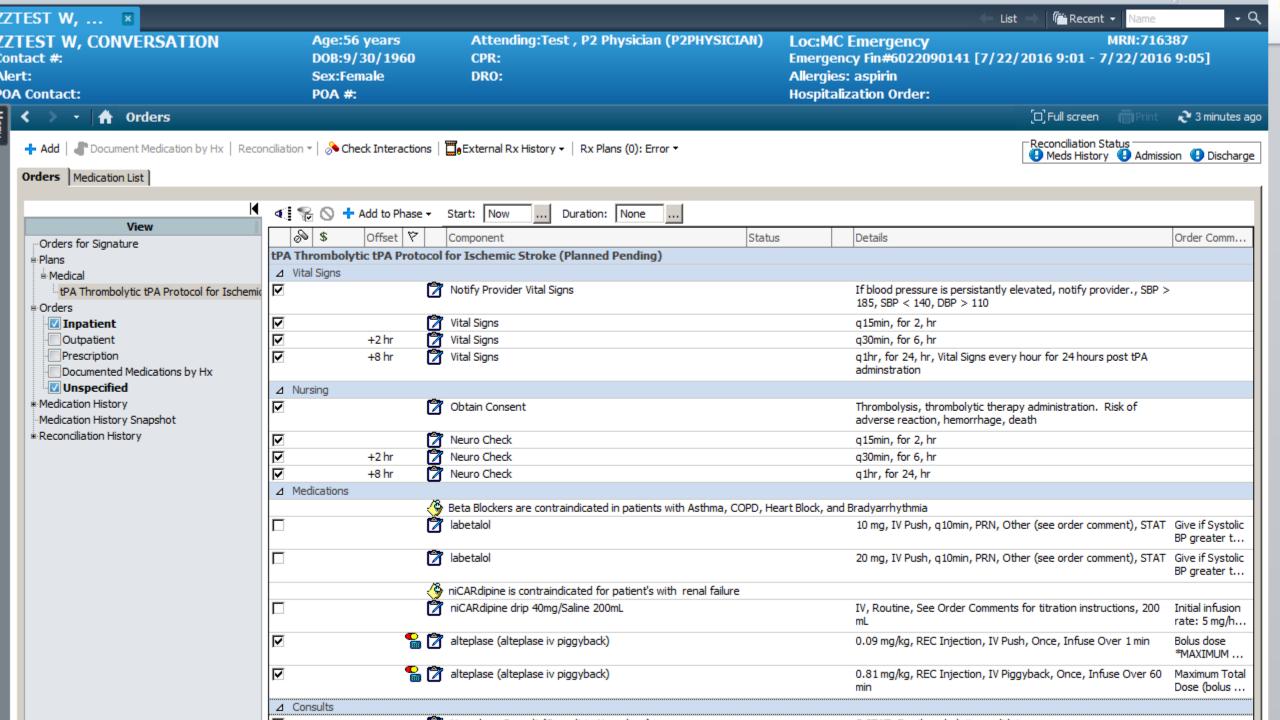
"Virinted as advisory for clinical decision making and may not be all-inclusive or definitive. (Could be an absolute contraindication in fow-risk patients with myocardial infarction.

# Design orders to accomplish the task

- CT
- Labs
- Hypertension Control
- TPA
- Nursing Orders





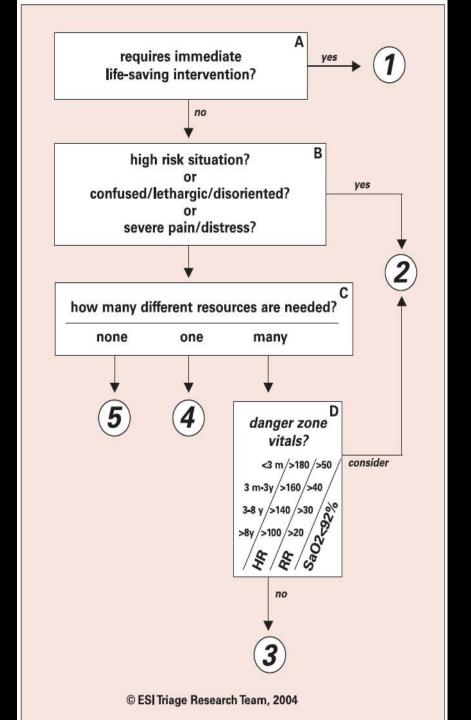


### Triage

- The process of sorting people based on their need for immediate **medical** treatment as compared to their chance of benefiting from such care. **Triage** is done in emergency rooms, disasters, and wars, when limited **medical** resources must be allocated to maximize the number of survivors.
- Why is the word quickly nowhere in this definition.

### Goals of Triage? (Trinity P & P)

- Rapid identification of patients with urgent, life threatening conditions.
- Quick sorting and determination of most appropriate treatment area
- Decrease Congestion of emergency department waiting
- Provide ongoing assessment of each patient
- Provide information to patients and families regarding care and waiting times
- Contribute information that helps to define departmental acuity



# You take a deep breath...Now what

- Back from CT
- Orders entered
- Blood in Lab
- Pharmacy alerted
- EMS alerted

- All of the details you rushed through.
  - Complete history and physical including detailed neurologic exam.
  - Review of Medications
  - Review of contraindications.
  - Discussion of Risk and benefits
- Consult with Neurologist



### Trinity Health Stroke Program In-House Follow up Tool

This information is provided for educational purposes only. No patient identifying information is included in this report

Date: 9/8/16 Referring Agency/Facility: New Town EMS/No Star

Last Known Well: 1720 Patient arrival time: 1844
Stroke Alert called: 1825 Patient's FIN: # 165202580

Stroke Alert Metric	Goal	Actual	Met/Not Met
DOOR TO MD	10 minutes	0 Minutes	
EVALUATION			
DOOR TO CT SCAN	25 minutes	13 Minutes	
CT SCAN TO RESULTS	20 minutes	31 Minutes	-
DOOR TO LAB RESULTS	45 minutes	PTA	
DOOR TO MEDICATION ORDER:		48 Minutes	
DOOR TO NEEDLE	60 minutes	57 Minutes	

### Staff involved:

ETC: Dr. Talley, Patti H. RN

NEUROLOGIST: Dr. Kordlar

### **Comments:**

Patient arrived via Northstar from New Town; he was quickly evaluated and sent to CT. This was negative and he was a candidate for thrombolytics. The patient was not sure if he wanted to receive the medication, so there was a slight delay in giving him the medication based on getting his consent. He did receive it within the 60 minute time frame. Great Job!

# Neuro Assessment of Acute Stroke

Cory Edwards, MD

Altru Health System

### Is This a Stroke?

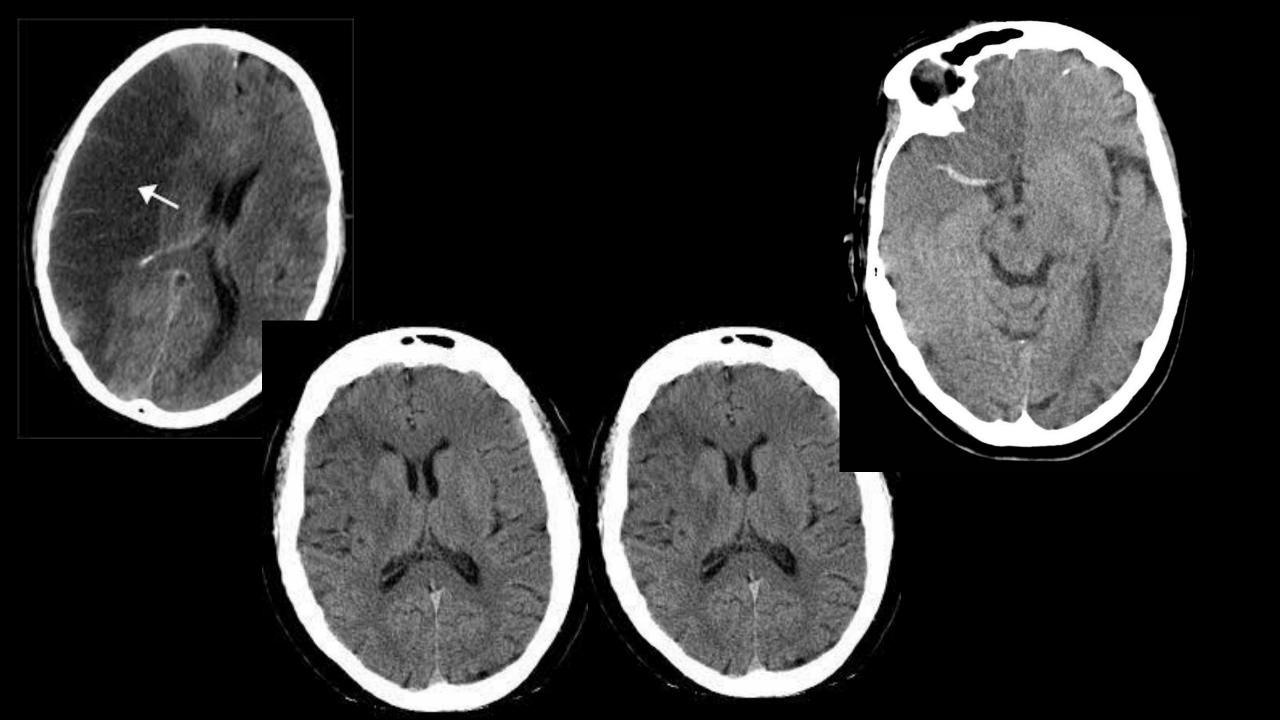
- Focal Neurological symptoms
  - Acute onset
- Differentials?
  - Stroke/TIA. Seizure. Migraine equivalent. Hypoglycemia. Psychogenic. Mass lesion. Delirium.....
  - When main symptom is Encephalopathy, very difficult to ascertain.
    - Is there focal findings? Insulin use? Epilepsy? Drug use? Trauma?
- Confusing symptoms.
  - Crossed findings in the brainstem
  - Total facial paralysis
  - Brainstem symptoms not well represented on stroke scale
- ABC's are always initial Assessment (ER Team)
- STAT labs and EKG
  - Discuss later that most labs should not delay administration of TPA

### TPA considerations

- Last Known Well
  - May not be able to determine exact time of onset
  - Very crucial
  - Largely determines whether or not Alteplase candidate
  - Within 3 hours vs the 3-4.5 hour time window
  - Consideration for Neuro Intervention
  - Many different ways to figure out times (cell phones, TV shows.....)

### Consideration Cont.

- Need to know BP
  - If from outside hospital, this could be treated early and hopefully stable within goal by the time arrived at receiving facility
- Medication List
- History of Diabetes and/or Stroke
- Head CT early
  - If signs of hemorrhage, not a candidate for further stroke intervention
  - Look for evidence of extensive stroke, mild early changes, or dense artery sign



### 3 Hour Time Window

- < 3 hours
  - Age 18 or higher

Exclusion criteria			
Historical			
Significant stroke or head trauma in the previous three months			
Previous intracranial hemorrhage			
Intracranial neoplasm, arteriovenous malformation, or aneurysm			
Recent intracranial or intraspinal surgery			
Arterial puncture at a noncompressible site in the previous seven days			
Clinical			
Symptoms suggestive of subarachnoid hemorrhage			
Persistent blood pressure elevation (systolic ≥185 mmHg or diastolic ≥110 mmHg)			
Serum glucose <50 mg/dL (<2.8 mmol/L)			
Active internal bleeding			
Acute bleeding diathesis, including but not limited to conditions defined in 'Hematologic'			
Hematologic			
Platelet count <100,000/mm <sup>3</sup> *			
Current anticoagulant use with an INR >1.7 or PT >15 seconds*			
Heparin use within 48 hours and an abnormally elevated aPTT*			
Current use of a direct thrombin inhibitor or direct factor Xa inhibitor with evidence of anticoagulant effect by laboratory tests such as aPTT, INR, ECT, TT, or appropriate factor Xa activity assays			
Head CT scan			
Evidence of hemorrhage			
Extensive regions of obvious hypodensity consistent with irreversible injury			

### 3 Hours continued

### Relative exclusion criteria ¶

Only minor and isolated neurologic signs

Rapidly improving stroke symptoms

Major surgery or serious trauma in the previous 14 days

Gastrointestinal or urinary tract bleeding in the previous 21 days

Myocardial infarction in the previous three months

Seizure at the onset of stroke with postictal neurologic impairments

Pregnancy

- Many of these, TPA would be considered by many providers.
  - Risk Benefit ratio
  - If deficit is persistent and debilitating consensus to treat
    - Hemianopia
    - Aphasia
    - Visual or sensory extinction
    - Weakness limiting gravity effort
    - Any deficits considered potentially disabling

### 3-4.5 Hours

- All exclusion criteria noted earlier for < 3 hours, PLUS....
  - Age > 80
  - Oral Anticoagulant use regardless of INR
  - Severe stroke (NIHSS > 25)
  - Combination of both prior clinical stroke and diabetes

### Timing of TPA

- Improving timing
  - Accurate weight (bed scale, weigh bed/patient together.....)
  - Head CT immediately on any potential code stroke
  - STAT labs
  - Finger stick for glucose
  - Frequent BP monitoring
- Lab work: Only need to know glucose prior to TPA unless.....
  - history of bleeding or on anticoagulation
  - If history of thrombocytopenia or bleeding abnormality
  - Anticoagulant/Medication list is not known
  - Many places would order/start Alteplase while waiting for labs
    - Consider stopping depending on laboratory abnormalities
- Use of newer Anticoagulants
  - TPA generally not recommended unless have not taken in 24-48 hours

### Delays in Treatment

- Most delay is prior to any hospital
  - Live alone, go to PCP, talk with family members
  - Feel they can "sleep it off".....
  - 911!!!!! Is always the best course of action
- Head CT
  - Biggest delay in hospital
  - Immediately to head CT
  - Conversations with interpreting radiologist or stroke neurologist personal interpretation
- Goal is < 60 minutes door to needle</li>
  - Alteplase at bedside
  - Not waiting on coag tests
  - If stroke physician comfortable reading head CT
  - Do not need written consent
  - Telemedicine stroke neurologist immediately available

### NIH Stroke Scale

1a. Level of consciousness: The investigator must choose a response if a full evaluation is prevented by such obstacles as an endotracheal tube, language barrier, orotracheal trauma/bandages. A 3 is scored only if the patient makes no movement (other than reflexive posturing) in response to noxious stimulation.

- 0 = Alert; keenly responsive.
- 1 = Not alert; but arousable by minor stimulation to obey, answer, or respond.
- 2 = Not alert; requires repeated stimulation to attend, or is obtunded and requires strong or painful stimulation to make movements (not stereotyped).
- 3 = Responds only with reflex motor or autonomic effects or totally unresponsive, flaccid, and areflexic.
- the month and his/her age. The answer must be correct there is no partial credit for being close. Aphasic and stuporous patients who do not comprehend the questions will score 2. Patients unable to speak because of endotracheal intubation, orotracheal trauma, severe dysarthria from any cause, language barrier, or any other problem not secondary to aphasia are given a 1. It is important that only the initial answer be graded and that the examiner not "help" the patient with verbal or non-verbal cues
- 0 = Answers both questions correctly.
- 1 = **Answers** one question correctly.
- 2 = **Answers** neither question correctly.

1c. LOC commands: The patient is asked to open and close the eyes and then to grip and release the non-paretic hand. Substitute another one step command if the hands cannot be used. Credit is given if an unequivocal attempt is made but not completed due to weakness. If the patient does not respond to command, the task should be demonstrated to him or her (pantomime), and the result scored (ie, follows none, one or two commands). Patients with trauma, amputation, or other physical impediments should be given suitable one-step commands. Only the first attempt is scored.

- 0 = **Performs** both tasks correctly.
- 1 = **Performs** one task correctly.
- 2 = Performs neither task correctly.

- 2. Best gaze: Only horizontal eye movements will be tested. Voluntary or reflexive (oculocephalic) eye movements will be scored, but caloric testing is not done. If the patient has a conjugate deviation of the eyes that can be overcome by voluntary or reflexive activity, the score will be 1. If a patient has an isolated peripheral nerve paresis (CN III, IV or VI), score a 1. Gaze is testable in all aphasic patients. Patients with ocular trauma, bandages, pre-existing blindness, or other disorder of visual acuity or fields should be tested with reflexive movements, and a choice made by the investigator. Establishing eye contact and then moving about the patient from side to side will occasionally clarify the presence of a partial gaze palsy.
- 0 = Normal.
- 1 = Partial gaze palsy; gaze is abnormal in one or both eyes, but forced deviation or total gaze paresis is not present.
- 2 = **Forced deviation**, or total gaze paresis not overcome by the oculocephalic maneuver.

- 3. Visual: Visual fields (upper and lower quadrants) are tested by confrontation, using finger counting or visual threat, as appropriate. Patients may be encouraged, but if they look at the side of the moving fingers appropriately, this can be scored as normal. If there is unilateral blindness or enucleation, visual fields in the remaining eye are scored. Score 1 only if a clear-cut asymmetry, including quadrantanopia, is found. If patient is blind from any cause, score 3. Double simultaneous stimulation is performed at this point. If there is extinction, patient receives a 1, and the results are used to respond to item 11.
- 4. Facial palsy: Ask or use pantomime to encourage the patient to show teeth or raise eyebrows and close eyes. Score symmetry of grimace in response to noxious stimuli in the poorly responsive or non-comprehending patient. If facial trauma/bandages, orotracheal tube, tape or other physical barriers obscure the face, these should be removed to the extent possible.

- 0 = No visual loss.
- 1 = Partial hemianopia.
- 2 = Complete hemianopia.
- 3 = **Bilateral hemianopia** (blind including cortical blindness).

- 0 = Normal symmetrical movements.
- 1 = **Minor paralysis** (flattened nasolabial fold, asymmetry on smiling).
- 2 = Partial paralysis (total or near-total paralysis of lower face).
- 3 = Complete paralysis of one or both sides (absence of facial movement in the upper and lower face).

- 5. Motor arm: The limb is placed in the appropriate position: extend the arms (palms down) 90 degrees (if sitting) or 45 degrees (if supine). Drift is scored if the arm falls before 10 seconds. The aphasic patient is encouraged using urgency in the voice and pantomime, but not noxious stimulation. Each limb is tested in turn, beginning with the non-paretic arm. Only in the case of amputation or joint fusion at the shoulder, the examiner should record the score as untestable (UN), and clearly write the explanation for this choice.
- 6. Motor leg: The limb is placed in the appropriate position: hold the leg at 30 degrees (always tested supine). Drift is scored if the leg falls before 5 seconds. The aphasic patient is encouraged using urgency in the voice and pantomime, but not noxious stimulation. Each limb is tested in turn, beginning with the non-paretic leg. Only in the case of amputation or joint fusion at the hip, the examiner should record the score as untestable (UN), and clearly write the explanation for this choice.

- 0 = No drift; limb holds 90 (or 45) degrees for full 10 seconds.
- 1 = Drift; limb holds 90 (or 45) degrees, but drifts down before full 10 seconds: does not hit bed or other support.
- 2 = Some effort against gravity; limb cannot get to or maintain (if cued) 90 (or 45) degrees, drifts down to bed, but has some effort against gravity.
- 3 = No effort against gravity; limb falls.
- 4 = No movement.
- UN = Amputation or joint fusion, explain:
- 5a. Left arm
- 5b. Right arm
- 0 = No drift; leg holds 30-degree position for full 5 seconds.
- 1 = Drift; leg falls by the end of the 5-second period but does not hit bed.
- 2 = Some effort against gravity; leg falls to bed by 5 seconds, but has some effort against gravity.
- 3 = No effort against gravity; leg falls to bed immediately.
- 4 = No movement.
- UN = Amputation or joint fusion, explain:
- 6a. Left leg

7. Limb ataxia: This item is aimed at finding evidence of a unilateral cerebellar lesion. Test with eyes open. In case of visual defect, ensure testing is done in intact visual field. The finger-nose-finger and heel-shin tests are performed on both sides, and ataxia is scored only if present out of proportion to weakness. Ataxia is absent in the patient who cannot understand or is paralyzed. Only in the case of amputation or joint fusion, the examiner should record the score as untestable (UN), and clearly write the explanation for this choice. In case of blindness, test by having the patient touch nose from extended arm position.

0 = Absent.

1 = Present in one limb.

2 = Present in two limbs.

UN = **Amputation** or joint fusion, explain:

- 8. Sensory: Sensation or grimace to pinprick when tested, or withdrawal from noxious stimulus in the obtunded or aphasic patient. Only sensory loss attributed to stroke is scored as abnormal and the examiner should test as many body areas (arms [not hands], legs, trunk, face) as needed to accurately check for hemisensory loss. A score of 2, "severe or total sensory loss," should only be given when a severe or total loss of sensation can be clearly demonstrated. Stuporous and aphasic patients will, therefore, probably score 1 or 0. The patient with brainstem stroke who has bilateral loss of sensation is scored 2. If the patient does not respond and is quadriplegic, score 2. Patients in a coma (item 1a=3) are automatically given a 2 on this item.
- 0 = Normal; no sensory loss.
- 1 = Mild-to-moderate sensory loss; patient feels pinprick is less sharp or is dull on the affected side; or there is a loss of superficial pain with pinprick, but patient is aware of being touched.
- 2 = Severe to total sensory loss; patient is not aware of being touched in the face, arm, and leg.

9. Best language: A great deal of information about comprehension will be obtained during the preceding sections of the examination. For this scale item, the patient is asked to describe what is happening in the attached picture, to name the items on the attached naming sheet and to read from the attached list of sentences. Comprehension is judged from responses here, as well as to all of the commands in the preceding general neurological exam. If visual loss interferes with the tests, ask the patient to identify objects placed in the hand, repeat, and produce speech. The intubated patient should be asked to write. The patient in a coma (item 1a=3) will automatically score 3 on this item. The examiner must choose a score for the patient with stupor or limited cooperation, but a score of 3 should be used only if the patient is mute and follows no one-step commands.

- 0 = No aphasia; normal.
- 1 = Mild-to-moderate aphasia; some obvious loss of fluency or facility of comprehension, without significant limitation on ideas expressed or form of expression. Reduction of speech and/or comprehension, however, makes conversation about provided materials difficult or impossible. For example, in conversation about provided materials, examiner can identify picture or naming card content from patient's response.
- 2 = **Severe aphasia**; all communication is through fragmentary expression; great need for inference, questioning, and guessing by the listener. Range of information that can be exchanged is limited; listener carries burden of communication. Examiner cannot identify materials provided from patient response.
- 3 = Mute, global aphasia; no usable speech or auditory comprehension.

10. Dysarthria: If patient is thought to be normal, an adequate sample of speech must be obtained by asking patient to read or repeat words from the attached list. If the patient has severe aphasia, the clarity of articulation of spontaneous speech can be rated. Only if the patient is intubated or has other physical barriers to producing speech, the examiner should record the score as untestable (UN), and clearly write an explanation for this choice. Do not tell the patient why he or she is being tested.

11. Extinction and inattention (formerly neglect): Sufficient information to identify neglect may be obtained during the prior testing. If the patient has a severe visual loss preventing visual double simultaneous stimulation, and the cutaneous stimuli are normal, the score is normal. If the patient has aphasia but does appear to attend to both sides, the score is normal. The presence of visual spatial neglect or anosognosia may also be taken as evidence of abnormality. Since the abnormality is scored only if present, the item is never untestable.

0 = Normal.

1 = Mild-to-moderate dysarthria; patient slurs at least some words and, at worst, can be understood with some difficulty.

2 = Severe dysarthria; patient's speech is so slurred as to be unintelligible in the absence of or out of proportion to any dysphasia, or is mute/anarthric.

UN = **Intubated** or other physical barrier, explain:\_\_\_\_\_

- 0 = No abnormality.
- 1 = Visual, tactile, auditory, spatial, or personal inattention or extinction to bilateral simultaneous stimulation in one of the sensory modalities.
- 2 = Profound hemi-inattention or extinction to more than one modality; does not recognize own hand or orients to only one side of space.



You know how.

Down to earth.

I got home from work.

Near the table in the dining room.

They heard him speak on the radio last night.

**MAMA** 

TIP - TOP

FIFTY - FIFTY

**THANKS** 

**HUCKLEBERRY** 

**BASEBALL PLAYER** 

## **NIHSS**

### Pros

### Cons

- Relatively easy to use and train
- Clinical Care and Research purposes
- Repeatedly validated
  - Assessing stroke severity and potential outcomes
  - Predicts damaged brain volume
  - Higher scores = higher risk of hemorrhagic conversion
- Tele medicine
- Assess changes in exam

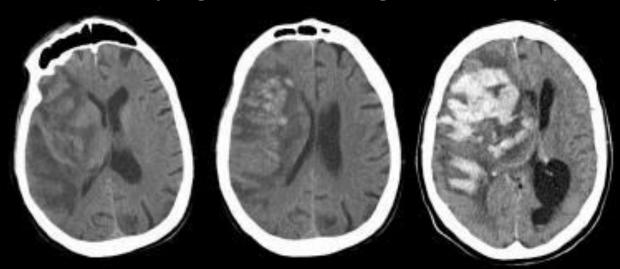
- Does not identify all stroke related impairments
- Posterior (VB) circulation poorly represented
  - Dysphagia, diplopia, balance, ataxia, vertigo.
- Many things limited by mental status and aphasia
- Interrater reliability
  - Facial, ataxia, neglect, dysarthria

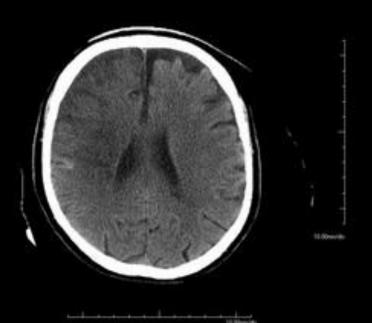
### Acute Treatment

- If patient's eligible and agreeable, treatment with IV Alteplase recommended
  - Informed consent.....
  - Within 3 hours = Grade 1A evidence. 3-4.5 hours = Grade 2A evidence
- Dosage = 0.9 mg/kg (actual body weight) with a max dose of 90 mg.
  - 10% as bolus over 1 minute, remaining 90% over one hour
  - Accurate weight important
- Withhold Alteplase if CT shows extensive multilobar hypodensity with > 33% of hemisphere.
  - Minor ischemic changes is NOT a contraindication (subtle or small hypodensity, loss of gray-white distinction, hyperdense artery sign, obscuration of lentiform nucleus)
- Time is brain sooner the treatment the better
- Strict BP control
  - At or below 185/110 prior to administration
  - At or below 180/105 for 24 hours post TPA

# TPA complications

- ICH
  - 5-7% for <u>symptomatic</u> ICH
  - Symptomatic?
    - Neurological worsening. Mostly 4 or more points on the NIHSS.
    - Would not count small petechial hemorrhages
  - No statistically significant change in mortality





## Complications Cont.

- Systemic Bleeding
  - Oozing for catheter, ecchymosis around BP Cuff, gum bleeding, subconjunctival.....
  - Rarely have to discontinue
    - If serious bleeding ..... GI, GU, Pericardial (MI)
    - If hypotension after TPA consider echo to r/o pericardial bleed
- Angioedema
  - 1-8%
  - Mild and transient
  - On affected side of body (opposite side of stroke)



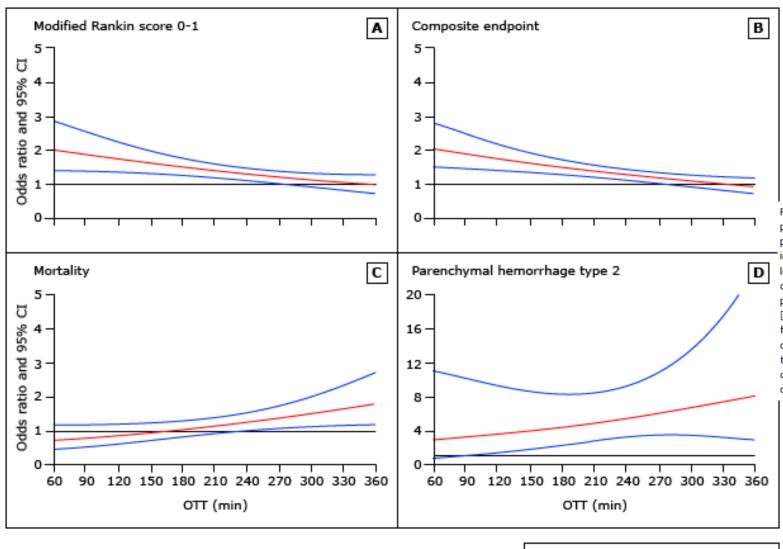
### Outcomes

- Time is brain
  - Benefit of intravenous thrombolysis decreases continuously over time from symptom onset
- Outcome with pooled data
  - Many trials (NINDS, ATLANTIS, ECASS 1, 2, 3, EPITHET and IST-3)
  - Primary outcome largely proportion achieving good outcome at 3-6 months determined by modified Rankin scale of 0 or 1.
  - Within 3 hours good outcome 33% vs 23% for control
  - 3-4.5 hours 35% vs 30 %
  - Alteplase beneficial regardless of patient age, stroke severity, or the associated increased risk of symptomatic or fatal intracranial hemorrhage in the first days after Alteplase treatment

### Modified Rankin scale

Score	Description
0	No symptoms at all
1	No significant disability despite symptoms; able to carry out all usual duties and activities
2	Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance
3	Moderate disability; requiring some help, but able to walk without assistance
4	Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance
5	Severe disability; bedridden, incontinent, and requiring constant nursing care and attention
6	Dead

#### Stroke treatment delay and outcome



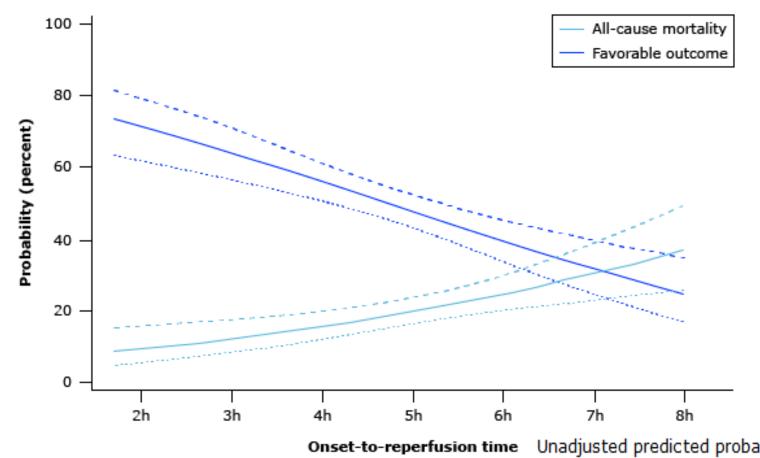
Relation of stroke onset to start of treatment (OTT) with treatment effect after adjustment for prognostic variables assessed by A) day 90 modified Rankin score 0-1 versus 2-6 (interaction p=0.0269, n=3530 [excluding EPITHET data p=0.0116, n=3431]); B) global test that incorporates modified Rankin score 0-1 versus 2-6, Barthel Index score 95-100 versus 90 or lower and NIHSS score 0-1 versus 2 or more (interaction p=0.0111, n=3535 [excluding EPITHET data p=0.0049, n=3436]); C) mortality (interaction p=0.0444, n=3530 [excluding EPITHET data p=0.0582, n=3431]); and D) parenchymal hemorrhage type 2 (interaction p=0.4140, n=3531 [excluding EPITHET data p=0.4578, n=3431]). Thus, for parenchymal hemorrhage type 2, the fitted line is not statistically distinguishable from a horizontal line. For each graph, the adjusted odds ratio is shown with the 95% CIs. CIs from the models will differ from those shown in the tables because the model uses data from all patients treated within 0-360 min whereas the categorized analyses in the tables are based on subsets of patients: the modeled CIs are deemed to be more reliable.

Odds ratio estimated by model
 95% CI for estimated odds ratio

## Mechanical Thrombectomy

- Consideration for patients when groin puncture can be obtained within 6 hours of last known normal and NIHSS 6 or greater
  - Most likely to have large vessel occlusion
  - Many would consider with lower scale depending on age and deficits
- Can also be considered for patient's who are not Alteplase candidates for whatever reason
- Many recent trials supporting this
  - SWIFT PRIME, ESCAPE, MR CLEAN, EXTEND-IA, REVASCAT
- Should receive Alteplase without delay even if thrombectomy considered early on (i.e. dense artery sign).
- Again Time is Brain

## Probability of mortality and favorable outcome at 90 days by stroke onset-to-reperfusion time



Unadjusted predicted probability of mortality and favorable outcome at 90 days by onset-to-reperfusion time following endovascular therapy for acute ischemic stroke. Solid lines represent the probability of outcome (light blue: all-cause mortality; dark blue: favorable outcome) over onset-to-reperfusion time (ORT) as predicted by unadjusted logistic regression model with ORT used as a continuous variable. Dashed lines show the 95% confidence intervals.

%: percent.

## Wake Up Strokes

- Active Trials (MR Witness.....)
- No RCT's for Alteplase in these situations
  - Unable to provide evidence based treatments
- Currently most institutions would not recommend Alteplase in these situations unless LKW was within appropriate time windows
  - Many places considering neuro IR procedures depending on advanced imaging
  - Rapid MRI (diffusion, FLAIR, MRA TOF) or CTA/MRI or MR/CT perfusion
  - If evidence for penumbra and large vessel occlusion consideration

Acronym	Study Population	Investigational Treatment	Comparator	Imaging Concept	Further Imaging Exclusion Criteria	Planned Sample Size	
DAWN	Late onset stroke incl. unknown time of symptom onset	Endovascular (Trevo thrombectomy procedure)±IV tPA	Standard of care	Proximal occlusion; clinical-imaging mismatch: high NIHSS score with small DWI/CTP-rCBF lesion	Large ischemic lesion >1/3 MCA	500	
ECASS- 4:EXTEND	Stroke onset 4.5–9 h incl. unknown time of symptom onset	IV tPA (Alteplase 0.9 mg/kg)	Placebo	Penumbral: MRI	DWI lesion >1/3 MCA/>100 mL	264	
THAWS <sup>40</sup>	Unknown time of symptom onset	IV tPA (Alteplase 0.6 mg/kg)	Placebo	Estimati lesion a DWI–FL misma	age: _AIR A	DWI SPECTS <5	300
WAKE-UP <sup>41</sup>	Unknown time of symptom onset	IV tPA (Alteplase 0.9 mg/kg)	Placebo	Estimati lesion a DWI–FL misma	age: .AIR M	WI lesion >1/3 CA/>100 mL	800

EXTEND <sup>38</sup>	Stroke onset 4.5–9 h incl. unknown time of symptom onset	IV tPA (Alteplase 0.9 or 0.6 mg/kg)	Placebo	Penumbral: MRI or CTP	Infarct core >1/3 MCA/>70 mL	400
MR WITNESS	Unknown time of symptom onset	IV tPA (Alteplase 0.9 mg/kg)	n.a.	Estimation of lesion age: DWI-FLAIR mismatch	>10 microbleeds	80
NORTEST <sup>39</sup>	Eligible for IV tPA+subgroup <4.5 h after symptom recognition	Intravenous TNK 0.4 mg/kg	IV tPA (Alteplase 0.9 mg/kg)	For wake-up stroke: estimation of lesion age: DWI-FLAIR mismatch	n.a.	954
POSITIVE	Stroke onset <12 h incl. unknown time of symptom	Endovascular (aspiration, stent retriever)	Standard of care	Proximal occlusion; penumbral: MRI or CTP	Infarct on CT >1/3 MCA or ASPECTS	750

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